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Management of synchronous phyllodes tumors with invasive breast carcinoma: A review of the literature and a case report breast

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ABSTRACT

Phyllodes tumor is a relatively infrequent diagnosis in breast pathology, and even less commonly it can be associated with synchronous invasive or *in situ* breast carcinoma. We present an unusual case of a borderline phyllodes tumor coexisting with invasive lobular carcinoma and lobular carcinoma *in situ*. A review of prior similar cases demonstrates that malignant phyllodes tumors may be more likely to be associated with both triple-negative breast carcinomas as well as other primary malignancies, and as such tend to have worse outcomes. Management strategies should be tailored to individual patients' pathology with this in mind.

1. Introduction

Phyllodes tumors are known to be rare entities in the realm of breast pathology, with incidences around 1 in 100,000 women, and comprising less than 1% of all breast tumors. This relative infrequency, combined with the fact that they can resemble fibroadenomas on both imaging and tissue sampling, makes phyllodes tumors a diagnostic challenge. Oftentimes they are initially misdiagnosed and treated as if they are benign entities, with the true diagnosis only coming to light on final pathology after complete surgical resection.

Though there is conflicting evidence on what surgical approach and margin width constitutes the best outcomes with respect to local recurrence and disease free survival, these tumors are typically treated with wide local excision, and margins >1 cm [1]. Still, it seems the primary factor for recurrence and metastasis of phyllodes tumors (PTs) is the characteristics of the tumor itself [1,2]. PTs can be subclassified into benign, borderline, and malignant, based on histopathologic features including stromal cellularity, atypia, and overgrowth, rounded *versus* infiltrative margins, mitotic counts, nuclear pleomorphism, and presence of necrosis [3]. Borderline and malignant PTs, which comprise around 15–25% and 5–15% of all PTs, respectively, tend to have the highest rates of local recurrence and metastasis [4].

Though it is exceedingly rare, there have been descriptions of PTs manifesting concurrently with both invasive and *in situ* breast carcinomas [5–24]. This further complicates treatment planning, as the appropriate management for two pathologically differently behaving tumor subtypes must be coordinated in the same patient. Given the rarity of these tumors coexisting, or combining with more aggressive phyllodes subtypes and invasive carcinoma, there is not enough data to predict outcomes or delineate best management. This paper will present a review of the literature and a case report of a patient who was found to have a borderline phyllodes tumor concurrent with multifocal invasive lobular carcinoma and lobular carcinoma *in situ*, and will review recent reports of similar cases with a focus on management and outcomes.

2. Case report

A 63 year old woman was found to have a lump in the upper outer quadrant of her left breast on routine physical exam. Her medical history was otherwise unremarkable, except for a mother who had breast cancer at age 55. She was sent for mammography, which demonstrated a lobulated 5.2 cm mass with well-defined borders in the upper outer breast quadrant, with scattered benign calcifications. Targeted ultrasound localized this solid lobulated mass at 2 o'clock, 5 cm from the nipple, with mild vascularity, and benign fatty axillary lymph nodes. Core biopsy of the mass demonstrated a fibroepithelial lesion with cellular stroma and pseudoangiomatous stromal hyperplasia. She then underwent an excisional biopsy of this mass, which on final pathology was initially read as a 4.2 cm fibroadenoma associated with multifocal infiltrating well-differentiated lobular carcinoma, 1.3 mm in size, as well as multifocal lobular carcinoma *in situ*, 1.5 cm in greatest dimension. The patient was then referred to our institution for a second opinion.

Her pathology slides were sent for a second opinion, which reported a 4.2 cm mass with moderate cellularity, intratumoral homogeneity,

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focal clefts and leaf-like architecture, prominent stromal vascularity, and an infiltrative edge. The spindle cells composing the lesion show up to 7 mitoses per 10 high power fields, all consistent with a borderline phyllodes tumor. In addition, there were at least 12 scattered foci of microinvasive and invasive lobular carcinoma, ranging in size from < 1 mm to 1.5 mm in greatest dimension, arising within the phyllodes. Extensive lobular carcinoma *in situ* was present within the phyllodes tumor (Figs. 1–3) and in adjacent breast tissue. The phyllodes tumor was < 1 mm from the posterior and inferior margins, while invasive carcinoma was 1 mm from the superior margin, with no lymphovascular invasion. The carcinoma stained strongly positive for ER and weakly positive for PR (Fig. 3B), with HER2/neu equivocal (2+) by immunohistochemistry but negative by FISH.

A postoperative MRI was done to assess for residual disease given the positive surgical margins and patient's desire for breast conservation. This demonstrated a 3.9 cm postsurgical cavity in the left breast with indeterminate enhancement extending inferiorly, representing either postsurgical change or residual tumor. After consultation at our institution, the patient elected to undergo nipple-sparing mastectomy with sentinel lymph node biopsy and immediate reconstruction with tissue expander. Final pathology demonstrated focal atypical lobular hyperplasia with no evidence of residual carcinoma or phyllodes tumor, and two axillary lymph nodes were negative for malignancy. She was started on Arimidex postoperatively and has since been doing well, with no evidence of disease 7 months after her surgery.

3. Discussion

In review of the literature from the last 17 years, shown in Table 1, there have been 22 case reports and 1 case series of 5 patients with phyllodes tumors (PTs) occurring in the same breast as various types of both invasive and *in situ* carcinomas, some with concomitant sarcomas [5–26]. Of note, although the case series from Sin et al. documented 10 patients, 5 patients were excluded from our review due to findings of only LCIS, opposite breast tumors, or axillary as opposed to breast cancer [26]. These patients had an average age of 52 (range 24–80). Of these 27 cases, 11 involved malignant PTs, 9 were benign, and, including ours, 7 were classified as borderline. Furthermore, 17 of the 27 cases (63%) describe PTs coexisting with invasive carcinomas, while 10 (37%) involved only *in situ* carcinoma. Three patients (11.1%) had a history of various sarcomas (liposarcoma, chondrosarcoma, osteosarcoma, and unspecified) in addition to their breast pathology, while 2 (7.4%) also had squamous carcinomas. Six of the 11 malignant PTs were associated with invasive breast carcinomas, while 5 of the 9 benign and 6 of 7 borderline PTs shared this characteristic. Interestingly, of the 5 reported triple negative carcinomas (and one reported as ER and PR negative with no comment on HER2), 4 were associated with malignant PTs and the other with borderline PT.

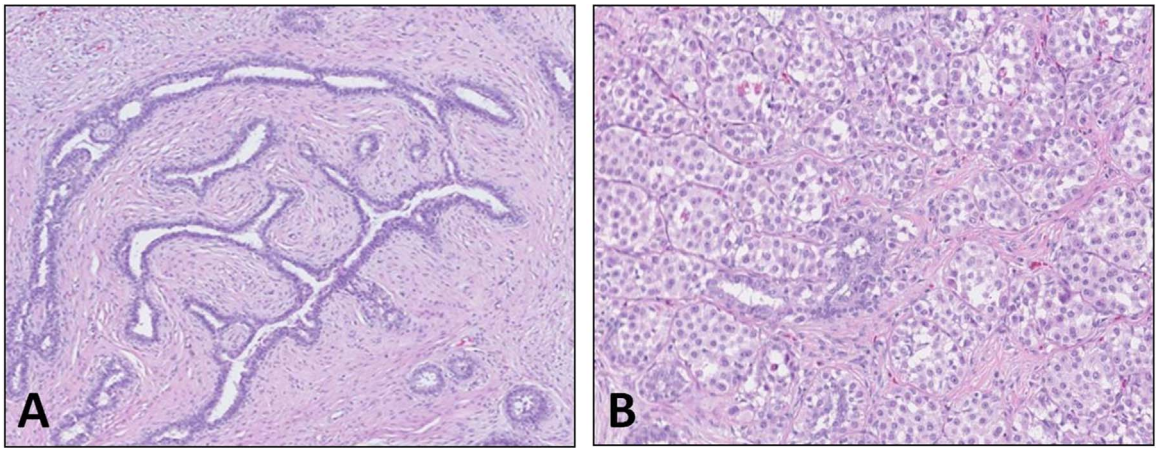

Fig. 1. A, Borderline phyllodes tumor. Hematoxin and Eosin stain 250×. B, Lobular carcinoma *in situ*. Hematoxin and Eosin stain, 200×.

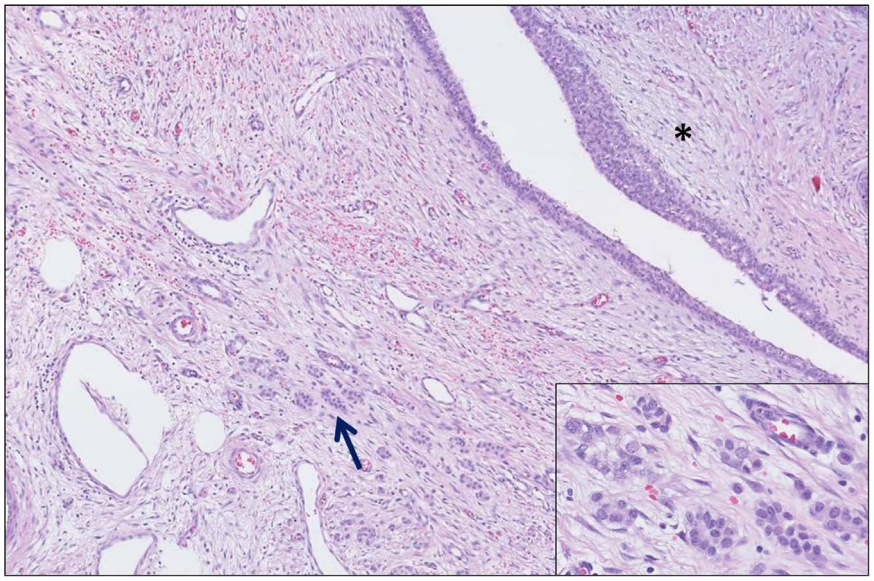

Fig. 2. Invasive lobular carcinoma (arrow) adjacent to phyllodes tumor (asterisk). Hematoxin and Eosin stain 100×. Inset, Invasive lobular component at 400×.